REMARKS

Claims 72 and 73 were examined in this case. Both claims have been objected to based on formalities and rejected under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 102(b). Each of these issues is addressed below.

Amendments

Claims 72 and 73 have been canceled, and new claims 74-93 have been added. Support for these new claims is found in the specification, for example, as follows: claim 74, page 4, ll. 22-25, page 5, ll. 1-3, and original claims 2 and 29; claim 75, original claim 3; claim 76, original claim 4; claim 77, original claim 5; claim 78, original claim 6; claim 79, original claim 7; claims 80 and 81, original claim 8; claim 82, original claim 9; claims 83 and 84, original claim 10; claim 85, original claim 11; claim 86, original claim 16; claim 87, original claim 17; claim 88, original claim 18; claim 89, original claim 19; claim 90, original claim 20; claim 91, original claim 21; and claims 92 and 93, original claim 22. These claims add no new matter.

Claim Objections

Claims 72 and 73 stand objected to on the basis that these claims depend on non-elected claims. Claims 72 and 73 have been canceled, but their language is now incorporated into new claims 74 and 75. These new claims no longer include dependencies to non-elected claims, and this objection may be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 72 and 73 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

These claims stand rejected first on the basis that they lack a method step or steps. New claim 74, which is based on claim 72, now includes such a method step. This

claim, which is directed to a "method for *reducing* the antigenicity of AAV" (rather than "altering" the antigenicity of AAV), specifies that the method be carried out by introducing at least one modification into the AAV structural protein, that modification reducing antigenicity without bringing about a negligible reduction in viral infectivity. As a method step is now included in claim 74, this basis for the rejection under 35 U.S.C. § 112, second paragraph may be withdrawn.

Claims 72 and 73 also stand rejected based on the assertion that "the metes and bounds of 'reduction' in antigenicity are not clearly defined in the specification" because the word "reduction" lacks comparative basis. This rejection is also overcome by the language of new claim 74. This claim indicates that the method results in "reduction in the antigenicity of the virus *relative to wild-type AAV.*" This basis for the rejection may also be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claims 72 and 73 stand further rejected under 35 U.S.C. § 102(b) as being anticipated by Mamounas *et al.* (WO 97/38723). As applied to the present claims, this rejection is respectfully traversed.

The present claims are directed to a method for reducing the antigenicity of AAV by introducing at least one modification into an AAV structural protein. This modification reduces viral antigenicity relative to the wild-type virus but brings about *only a negligible reduction in viral infectivity*. Nowhere is this claimed invention disclosed by Mamounas.

The Office points to page 4, lines 22-31, as describing Applicants' claimed invention, but this passage does not disclose that any mutated AAV structural protein is capable of supporting viral particle formation, as required by claim 74 and its dependent claims. Indeed, the only construct tested by Mamounas, as indicated at page 68, lines 13-14, "failed to produce any intact viral particles." In particular, Mamounas states (page 68,

ll. 14-18; emphasis added):

> To overcome this obstacle [the failure to produce any intact viral particles], we included *wild type AAV capsid proteins* into the packaging process. We employed a triple plasmid DNA co-transfection strategy, namely co-infecting cells with (1) *pAV/Ad [a rAAV vector encoding wild-type capsid protein; page 64, line 31]*, (2) pAAVgal conjugated to polylysine coupled adenovirus, and (3) the individual pVP-scFv chimeric protein-containing plasmid.

Thus, the only way that Mamounas could produce intact viral particles using this construct was to include in their transfection system a helper vector encoding wild-type capsid protein. That wild-type capsid protein was necessary for viral particle formation; the modified virus was not infective on its own.

In addition, Applicants point out that Mamounas does not discuss in any way a method for *reducing the antigenicity* of AAV; nor does Mamounas report changes in the antigenicity of modified AAV structural proteins. The Office contends that the virus of Mamounas is reduced in antigenicity. However, this is not indicated by the reference, which simply states that the AAV was modified in the VP1 or VP3 region for the purpose of changing viral *cell targeting*. This, of course, does not relate to the level of antigenicity of the virus for the host, but rather relates to the entirely different issue of the choice of cell targeted for viral entry.

Thus, Mamounas fails to describe a method for reducing the antigenicity of AAV while maintaining viral infectivity, as required by the present claims. The § 102(b) rejection may be withdrawn.

CONCLUSION

Applicant submits that the claims are in condition for allowance, and such action is respectfully requested.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 27 Jan 2005

Karen L. Elbing, Ph.D.
Reg. No. 35,238

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045